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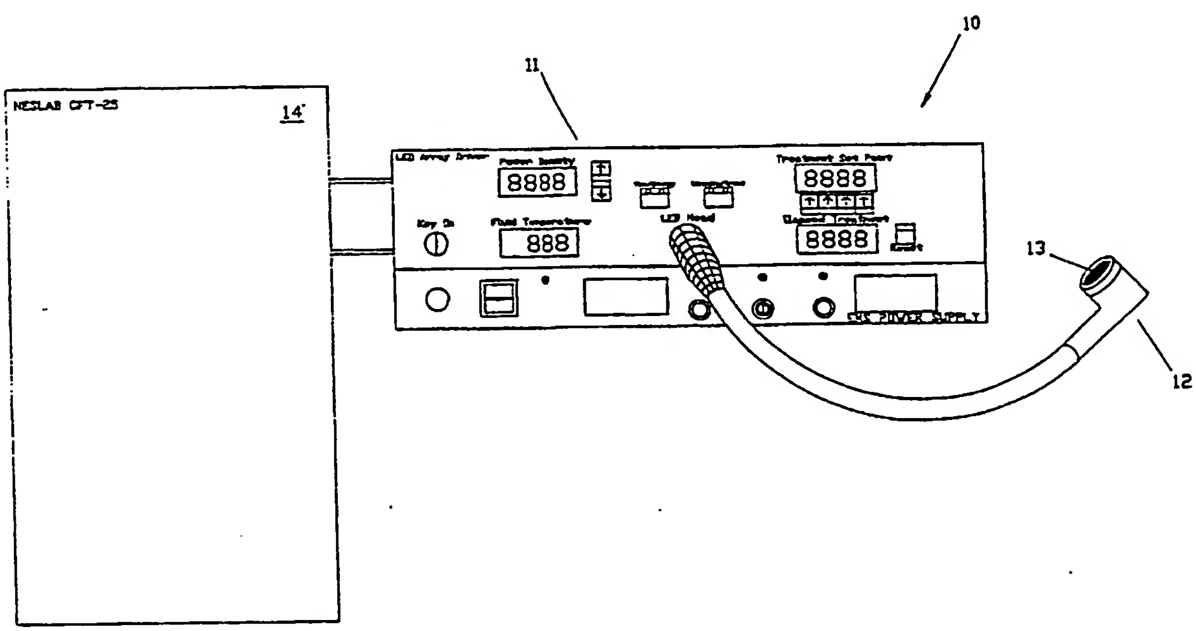

(57) Abstract

A system comprising a fluid cooled array of light emitting diodes (LEDs) for producing red (660 NM) light for photodynamic therapy is disclosed. The light is produced by a plurality of overdriven, water cooled LEDs arrayed on a preferably disposable puck. The LED puck (13) is releasably connected to an interchangeable LED hand piece (12). The system can be configured for illumination of flat surfaces such as for treatment of the chest or back, or for cylindrical surfaces such as found in the cervix or colon, by proper selection of the LED hand piece (12) and puck design (13).

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LIGHT EMITTING DIODE SOURCE FOR PHOTODYNAMIC THERAPY

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to photodynamic therapy and more specifically to a light source for photodynamic therapy.

2. Acknowledgement

This invention was made with Government support under Grant No. 1R43CA55446-1 awarded by the Department of Health and Human Services. The Government has certain rights in the invention.

3. Prior Art

Photodynamic therapy (PDT) is presently undergoing extensive basic pre-clinical and clinical testing and development both domestically and internationally. The general method of performing PDT is now well known and described, for example, in U.S. Patents 4,968,715; 4,932, 934; and 5,028,621 to Dougherty, et al.; and 5,002,962 to Pandey, et al. In PDT, photosensitizing drugs such as hematoporphyrin derivatives are introduced into and retained by the hyperproliferating cells or tissue such as cancerous tissue and atheromas. With the exposure to suitable wavelengths of light the photochemical reaction of the photosensitizer can lead to selective destruction of photosensitizer-associated cells or tissue. PDT also holds potential for a number of possible applications other than cancer treatment such as for treating microvascular lesions and blood purging. To obtain the desired therapeutic response, all of these applications require the delivery of sufficient light of appropriate wavelength to the photosensitizer <u>in vivo</u>. The

activating light must be sufficiently intense at wavelengths matching the absorption spectrum of the photosensitizer to initiate the photochemical reaction. Secondly, these wavelengths need to penetrate the host tissue to permit activation of the therapeutic reaction at the desired depth. Additionally, the light must be able to be delivered to the treatment area in sufficient quantities to permit treatment on a reasonable and effective time scale.

Prior art sources of illumination have been primarily lasers. The reasons for this are the efficient deliverability of the laser light through flexible single optical fibers, the single wavelength nature of the laser, the tunability of certain lasers, and the ability to deliver sufficient effective power to permit reasonable treatment times. All of these properties together have permitted PDT to be administered endoscopically with the interstitial delivery of the light for the treatment of otherwise inaccessible or large thick lesions. The use of lasers has not been without drawbacks. These negative qualities of the laser include high cost, low reliability, large size, complex operating procedures and constant attention to the safety issues required when dealing with laser light.

Puliafito, et al. (Arch. Ophthalmology, Vol 105, March, 1987) disclose using laser diodes for Photodynamic therapy. There are significant differences between LED's and laser diodes. A Light Emitting Diode (LED) is a solid state electronic device capable of emitting light when an electric current is passed through the device. LED-derived light is relatively broad band (20-40nm) and is emitted in a wide output distribution pattern, and

lacks coherence. The light is produced at very low current levels (20ma). All of these characteristics of LEDs serve to technically differentiate them from laser diodes. The major advantage gained by using a laser for PDT is the ability to couple significant light power into flexible optical waveguides. This is necessary for applications requiring interstitial or endoscopic delivery of treatment light for PDT. Laser diode systems which include a large power supply and cooling system are very expensive.

There are a significant number of applications for PDT that do not require the use of a laser light source or the delivery of light through light guides. In fact, the majority of the basic pre-clinical and original trials of PDT using hematoporphyrin derivative were done using non-laser light sources. For example the treatment of cutaneous and subcutaneous skin lesions less than 1.0 cm thick can be treated using non-laser light sources. Skin cancer incidence in the United States of America is over 550,000 new cases per year and rising. Even though a majority of these cases can be easily treated with local resection or other methods, there are a significant number involving multiple and/or recurrent lesions that could be more conveniently treated using PDT. The clinical use of PDT in many of these cases would be limited, in part, due to the need to use lasers. This is due to the high cost and lack of availability of suitable lasers. There is truly a need for a low cost non-laser light source for use in PDT.

There are a number of non-laser light sources that could potentially be used in certain PDT applications. The major properties of these light sources that determine their

applicability in PDT are: a) output spectrum; b) brightness or intensity at a suitable wavelength; c) deliverability; d) size; and e) cost. These non-laser light sources include arc lamps, incandescent lamps, fluorescent lamps and light emitting diodes (LEDs). The lamp sources have a broad emission spectrum ranging from ultraviolet to infrared. These broad spectrum sources require the use of optical filtering to remove the undesired wavelengths, particularly the ultraviolet and infrared, due to the potential of carcinogenic effects and heating respectively. In addition, the low brightness of these light sources at suitable wavelengths, compared to lasers, make them all poor candidates for transmitting sufficient power through small (less than 600 micron core), flexible light guide to effect PDT. The best of these light sources for brightness is the arc lamp due to the relatively high intensity and small size of the discharge arc. Even though such technology shows promise for certain medical applications, including PDT, it still suffers from problems such as the need for extensive filtering, limitations on its use for large area exposure, and the requirement for high voltage and the concomitant potential for arc lamp explosion.

LED technology, unlike the other non-laser light source outlined above, has the advantage of small size, typically 0.3 mm by 0.3 mm, limited emission spectrum band, typically 20 nm to 40 nm, high efficiency and low cost. The light power emitted from a single diode is relatively low however (approximately 4 milliwatts to 5 milliwatts for the brightest red LEDs using the specified driving currents) but its emission angle is low when compared, for

example, to the arc lamp so that its actual brightness is reasonably good. The small size of the LED along with its high efficiency give the potential of using an array consisting of multiple LEDs in a single device to significantly increase deliverable power density over a large area. The low power output has, however, delayed the acceptance of LED arrays as a suitable light source for PDT. The intensity can be increased by over-driving the LEDs in the array. Such over-driving results in heating which shortens the lifetime of the LED and causes a spectral shift in the output. LEDs are available in variety of discrete packages as well as several one and two-dimensional array packages. As used herein, an LED array means multiple LED's integrally mounted in a single device. Commercially available arrays, from manufacturers such as Mitsubishi, Hewlett Packard or Stanley Electric, combine a few LEDs in a single package but not in high enough packing density or in geometrics suitable for PDT. None of these prior art devices can provide sufficient power density for effective PDT treatments, nor can they be easily configured in the geometries necessary for the wide range of applications for surface illumination and PDT. It is desirable to have a multiple integrated LED array with a power output suitable for use in PDT.

SUMMARY OF THE INVENTION

It is an object of this invention to provide an array of multiple integrated LEDs useful for photodynamic therapy.

It is another object of the invention to provide an inexpensive light source useful for photodynamic therapy.

It is still another object of this invention to be able to provide an LED array for photodynamic therapy that is capable of illuminating the surface of various types of tissues.

It is yet a further object of this invention to provide an LED array for photodynamic therapy which enables accurate wavelength and exposure control and permits accurate dosimetry.

It is another object of this invention to provide an illuminating system for photodynamic therapy that is safe to both the physician and the patient.

The LED light source of the present invention is novel because it teaches how to use the characteristics of the LED to an advantage over the laser diode for applications of PDT which do not require interstitial or endoscopic light delivery. The wide output distribution pattern, small size, and minimal cooling requirements of the LED allow large arrays of the devices to be constructed which cumulatively are capable of producing a total output light power exceeding that of laser diodes. This opens up applications for large surface area illumination (such as is needed in dermatology) for which laser diode systems are inadequate.

These and other objects of the invention will soon become apparent as we turn now to a brief description of the drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic representation of an LED system suitable for illumination of surfaces for photodynamic therapy.

Figure 2 schematic diagram of the front panel of the LED array driver showing the displays for controls for exposure power and coolant temperature display.

Figure 3 is a cross-sectional view of the LED handpiece configured for flat surface illumination.

Figure 4 is a top view of the LED puck configured for flat surface illumination.

Figure 5, which is a detailed top view of the area shown in Figure 4 enlarged for ease of viewing, shows the top surface of the LED puck showing the machine holes and indicating the LED die.

Figure 6 is a cross-sectional view of the LED handpiece for illumination of cylindrical surfaces.

Figure 7 shows the LED sleeve for cylindrical surface illumination.

Figure 8 is a schematic diagram of a preferred embodiment of the light output and wavelength detector.

DESCRIPTION OF THE PREFERRED EMBODIMENT

It is the combination of small size and high efficiency that make the LED a potentially useful light source for PDT. The small size of the LED allows them to be fabricated in high density into applicators of various shapes for the direct contact treatment of cutaneous lesions. The shape may be circular, rectangular (or any curvilinear surface) for treating skin lesions or cylindrical for the treatment of cervical cancer. Planar arrays of LED's may be bent or folded to form various curvilinear surfaces to conform to the surface being treated. To be useful, the LED's must be overdriven to produce useful power outputs. The heat generated

during over-driving must be removed by cooling the LED in order to control the wavelength and increase the lifetime of the LED. Turning now to Figure 1, we see a schematic view of the LED system configured for flat surface illumination and generally indicated at the numeral 10. The system consists of the LED array driver 11, the flat surfaced LED handpiece 12, the flat surfaced LED puck 13 and the closed loop chiller 14. The detailed controls of the front panel of the system are shown in Figure 2 of the array driver 11, and shows the displays for the controls of exposure 21, power 22, the coolant temperature display 23 and the power supply 24.

An LED handpiece configured for flat surface illumination 12 is shown in cross section in Figure 3. The stainless steel housing 31 and threaded retaining ring 32 are connected to the system ground 33 and provide one electrical connection to the LED puck 13. The heat sink 34 is connected to the LED supply voltage 35. This provides the second electrical connections to the LED puck as well as removing the heat generated in the puck. The heat sink is electrically insulated from the housing by the DELRIN® insulator 36. The coolant tubes 37 provide a flow of cooling water from the chiller to the heat sink. The light output power and wavelength detector 38 (shown in greater detail in Figure 8) detects the amount of light being delivered to the patient by sensing the light through the light sense channel 39.

An LED puck configured for flat surface illumination is shown in Figure 4. The puck, generally indicated at 13, comprises a gold plated insulated copper and fiberglass laminate sheet 41 bonded to a flat copper substrate 42. Holes are machined through

the copper laminate to the surface of the copper substrate. The LED puck is coated with a clear epoxy potting material 43 to protect the LED device and provide a smooth clean surface for patient contact.

Figure 5, shown as detail A of Figure 4, is an enlarged view of the top surface of the LED puck showing the machined holes and indicating the LED die 51 bonded to the copper substrate 42 with electrically and thermally conductive epoxy 52. The figure also shows the gold bonding wire 53 attached between the top contact of the LED die and the surface of the copper laminate 41 using common integrated circuit assembly techniques.

Figure 6 shows a cross sectional view of the LED handpiece for illumination of cylindrical surfaces, generally indicated by 60. The stainless steel housing 31, threaded retaining ring 32, coolant tubes 37, the photodiode detector 34 and the insulator 36 function the same as in the flat surface illuminating handpiece. The heat sink 61, the light sense channel 62 and the LED sleeve 63 are now shaped appropriately for insertion into the cervical canal or rectum.

Figure 7 shows an LED sleeve configured for cylindrical surface illumination 63. The copper laminate 71, copper substrate 72 and LED 73 are assembled in a similar manner to the flat surface LED puck except the geometry is out of a tube instead of a disk.

The light output power and wavelength detector is shown in greater detail in Figure 8. The light transmitted through the light sense channel 39 (Figure 3) is focused by the collimating lens 81 and split into two equal light beams by the beamsplitter

82. The light power in one beam path is filtered by a filter 83, and measured by the photodiode 85. The unfiltered photodiode 84 measures the light power in the other light beam path. Assuming that proper calibration is done to compensate for the different optical losses in each path, the total optical power and verification of the wavelength can be accomplished with this technique. It is clear that this device could also be configured with a flexible light guide (not shown) built into the handpiece which would then deliver the sampled light energy to the light power output and wavelength detector shown in Figure 8 which could conveniently be installed in the LED array driver 11.

In summary, it has been shown that an LED array can be configured to provide power and wavelength outputs suitable for PDT. In order to achieve the required power levels, it is necessary to over-drive the LED's. The additional current required for over-driving generates heat at the diode junction which results in: (a) a red-shift and broadening of the output light; and (b) a shorter lifetime. To overcome these problems, the LED array is mounted on a puck enabling the LED array to be cooled to control the bandwidth and wavelength of the output light and increase the lifetime of the array. In practice, the output wavelength depends on the diode's junction temperature. Monitoring the wavelength permits adjustment of the coolant temperature and flow rate to maintain the junction at the desired temperature.

The foregoing preferred embodiment of the LED system for photodynamic therapy provides a low cost, high power excitation source for PDT which can be produced in a variety of shapes used

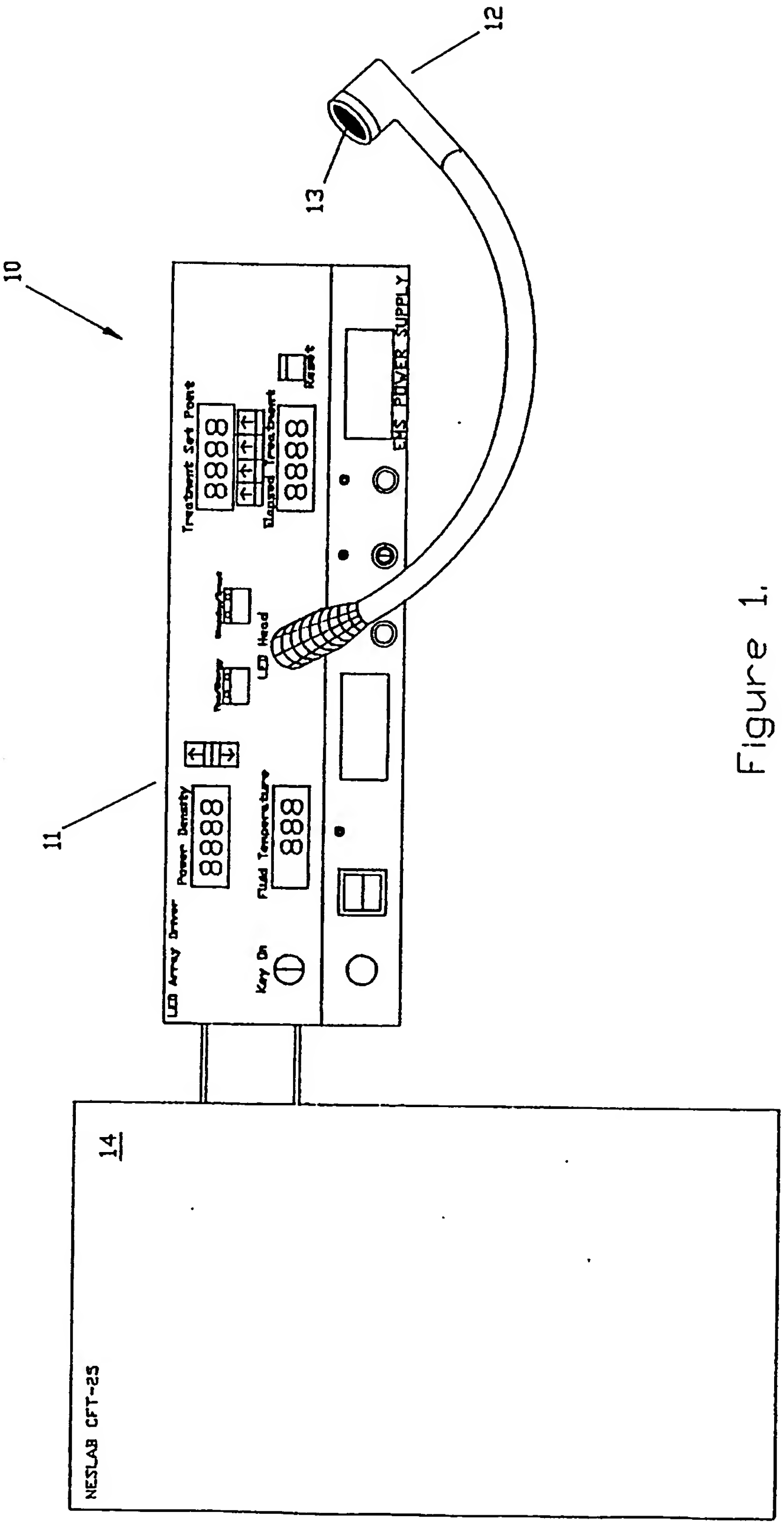
in a wide variety of applications. This device will allow PDT to become viable treatment modality for many more cancer patients inasmuch as it will now be cost effective for the physician's office or small clinic. Although the invention has been described in terms of particular embodiments and applications, one of ordinary skill in the art in the light of this teaching, can generate additional embodiments and modifications without departing from the spirit of or exceeding the scope of the claimed invention. For example, single LED chips may be fabricated into an array by depositing them directly onto a chilled substrate by techniques currently used in hybrid circuit fabrication. Accordingly, it is to be understood that the drawings and descriptions herein are preferred by way of example to facilitate comprehension of the invention and should not be construed to limit the scope thereof.

CLAIMS

What we claim is:

1. An incoherent light source suitable for administering illumination for photodynamic therapy, said incoherent light source comprising, in combination: a) an LED array driver; b) an LED array; and c) a cooling means.

2. The light source of Claim 1 wherein the LED array is in thermal communication with said cooling means.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11
12
13
14
LED Array Driver
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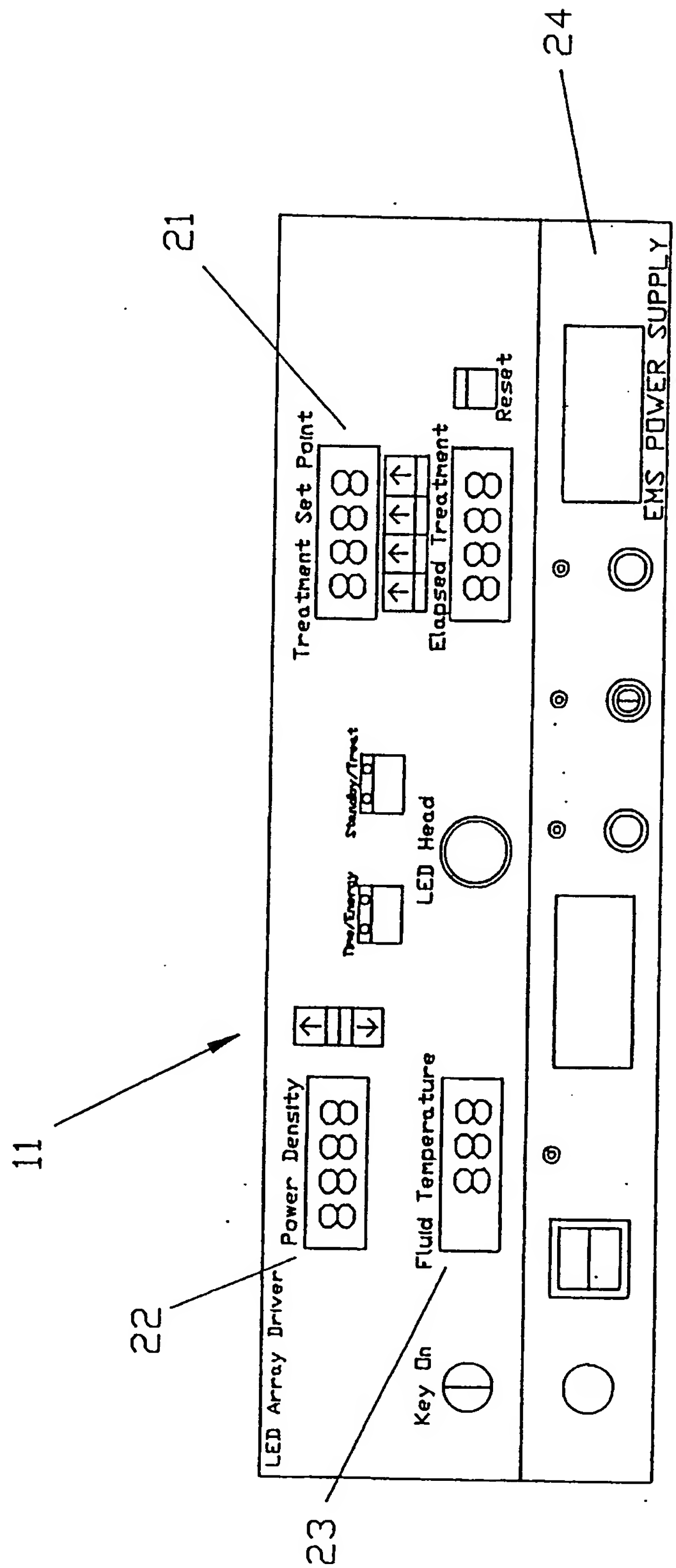
8888
Fluid Temperature
888
Key On
LED Head
Treatment Set Point
8888
Elapsed Treatment
8888
Reset
EMS POWER SUPPLY
NESLAB CFT-25

Figure 1.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8888
Fluid Temperature
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LED Array Driver
Key On
22
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Figure 2

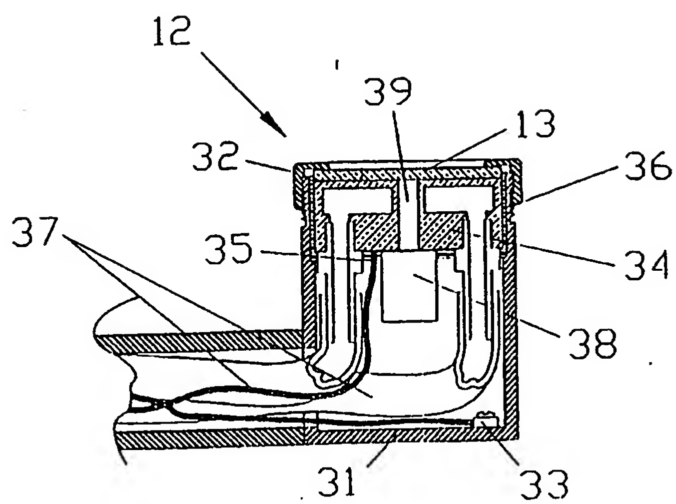

Figure 3.

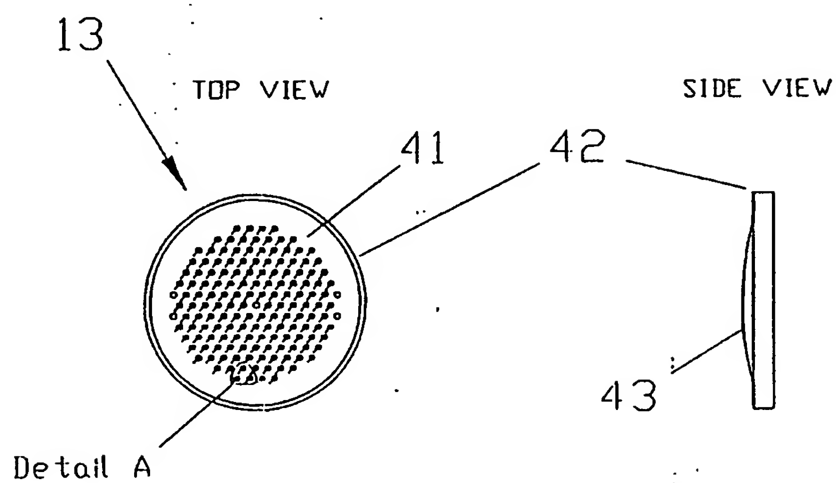

Figure 4.

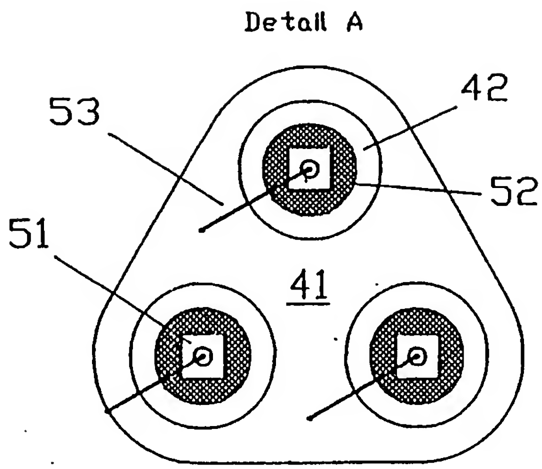

Figure 5.

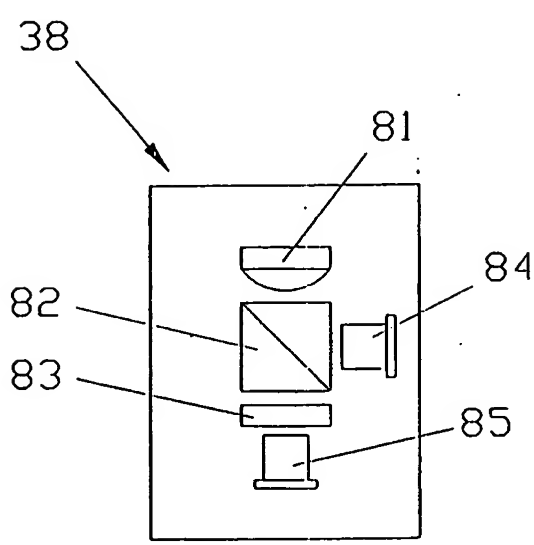

Figure 8.

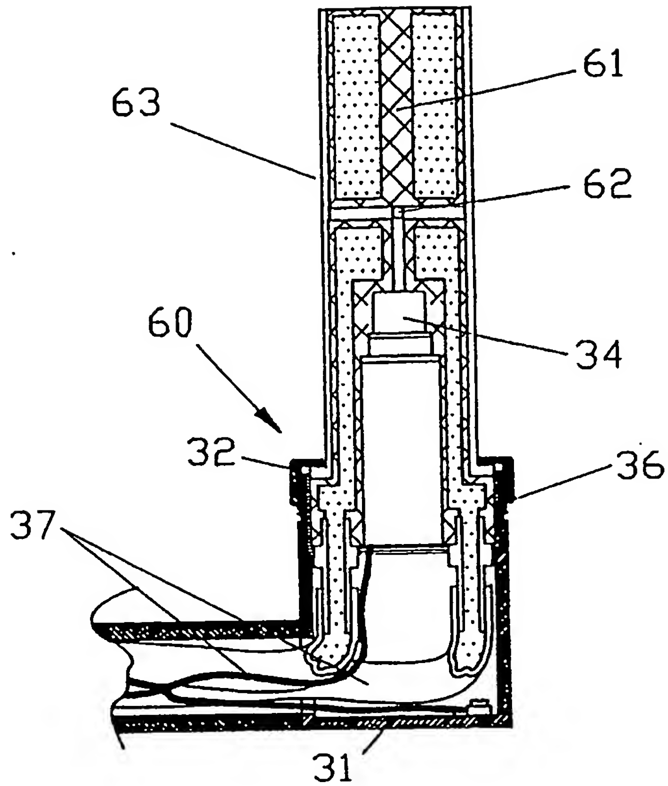

Figure 6.

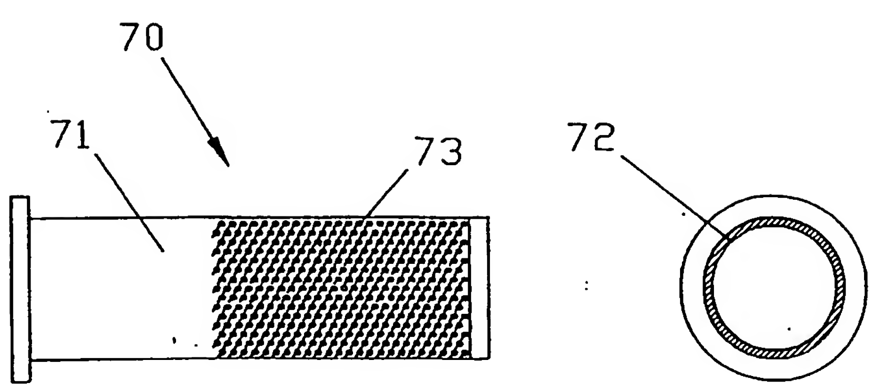

Figure 7.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/00506

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61N 1/00, 1/30, 5/00
US CL :128/395; 604/20; 606/4
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/395, 396; 514/410; 604/20; 606/4

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

None

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

None

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Journal of ARCH OPHTHAIMOL --- Vol 105, March 1987, pp. 424-427, Semiconductor Laser Endophotocoagulation of the Retina, CARMEN A. PULIAFITO, MD ET AL.	1-2
Y	US, A, 5,171,749, (LEVY ET AL.), 15 December 1992. See entire document.	2
A	GB, A, 2 212 010, (LISON ET AL.), 12 July 1989. See entire document.	

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
03 MARCH 1994	MAY 20 1994

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